

25
26Claims

1. A biologically active conjugate derivative having the following general formula (I)



where:

10 M represents the corresponding radical of a biologically active molecule selected from the group consisting of proteins, peptides and polypeptides;

FE represents a functionalizing entity selected from PEG, PVP, PacM, dextran, hormones, antibodies or antibody fragments; and

15 L represents a linking arm comprising a dipeptide selected from Met-Nle, Met-βAla, Gln-Gly, and Asp-Pro,

which is capable of being cleaved by chemical treatment to leave Nle, βAla, Gly or Pro, respectively, as a reporter group linked to M.

2. The biologically active conjugate derivative according to claim 1 characterised in that said functionalizing entity FE is a polymer with a molecular weight in the range of 2 Kd to 50 Kd.

25 3. The biologically active conjugate derivative according to claim 2 characterised in that said polymer is PEG.

30 4. The biologically active conjugate derivative according to claim 2 or 3 characterised in that said functionalizing entity FE is a linear polymer.

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Sub A1 7 5. The biologically active conjugate derivative according to claim 2 or 4 characterised in that said functionalizing entity FE is a branched polymer.

sub B2 6 6. The biologically active conjugate derivative according to claim 1 characterised in that said biologically active molecule is a protein selected from insulin, lysozyme, interferon, erithropoietin, G-CSF, GH.

7. A method for identifying linkage sites of conjugation of the functionalizing entity FE selected from PEG, PVP, PacM, dextran, hormones, antibodies or antibody fragments, on the biologically active drug conjugate derivative of claim 1, along the biologically active molecule M, which method comprises a specific chemical cleavage of the linking arm L comprising a dipeptide selected from Met-Nle, Met-βAla, Gln-Gly, and Asp-Pro, releasing after removing and separating FE by classical methods, to leave Nle, βAla, Gly or Pro, respectively, as a reporter group linked to M.

8. An intermediate compound, for the preparation of the biologically active conjugate of claim 1, having the following general formula (II)



where

FE represents a functionalizing entity selected from PEG, PVP, PacM, dextran, hormones, antibodies or antibody fragments; and

L represents a linking arm comprising a dipeptide selected from Met-Nle, Met-βAla, Gln-Gly, and Asp-Pro.

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